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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,866	05/29/2001	Brian Sorrentino	1340-1-021CIP2	4688

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EXAMINER
LI, QIAN J

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,866	SORRENTINO ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,17 and 21-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The amendment and response filed 3/4/03 have been entered as Paper No. 14. Claims 1-15 and 18-20 have been cancelled, claims 16 and 17 have been amended, and claims 21-28 are newly submitted. Claims 16, 17, and 21-28 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in paper #14 would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The prior rejection of claims 16 and 17 under 35 U.S.C. 102(a) as being anticipated by *Scheffer et al* (Proc Am Assoc Cancer Res 2000 Mar;41:page 803) is withdrawn in light of the newly submitted publication by Scheffer et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16 and 17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Ross et al* (US 6,313,277, IDS/AA), in view of *Niman et al* (US 5,563,247), and the rejection applies to newly submitted claims 21, 22, 25, and 26.

In paper #14, applicants argue that Ross teaches the preparation of antibodies using purified BCRP protein, which may recognize any portion of the protein. There is no teaching in Ross for generating antibodies, which will specifically recognize the extracellular portion of BCRP. Applicants further argue that a purified protein is different than the natural conformation required by the claims. Applicants additionally argue that Niman fails to teach any method for generating an antibody that recognizes an extracellular portion of a protein in its natural conformation, thus, *Niman* does not provide any additional teaching or suggestion sufficient to remedy the deficiencies of Ross.

The arguments have been fully considered but they are not persuasive for reasons of record in paper #13 and following.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re*

Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In the instant case, *Ross et al* teach that BCRP and its coding sequence is known, and the general method of producing and using an antibody specific to BCRP; and *Nieman et al* teach a method of producing a monoclonal antibody using a polypeptide and the resulting antibody could recognize the whole protein including the protein in its natural conformation.

First, *Ross et al* teach that a polyclonal antibody capable of binding to BCRP can be prepared by immunizing a mammal with a preparation of BCRP or functional derivative of BCRP (paragraph bridging columns 1 & 2), which encompass fragments containing the extracellular epitope, the antibodies produced by this method inherently comprising antibodies that recognize the extracellular portion of a BCRP. With respect to the natural conformation of a protein, a purified protein may or may not change its natural conformation. Neither the prior art nor the specification teaches that BCRP changes its natural conformation when purified.

Second, *Ross et al* also teach that the monoclonal antibody could be prepared by the method taught in reference 7 (column 4, line 50-57). A closer look of the reference, also not relied upon, *Kohler et al* (Eur J. Immunol 1976;6511-9) teach cell fusion between myeloma cells and antibody-producing cells, which were produced by immunizing mice with sheep red blood cells (whole cell including molecules on cell surface in its natural conformation), and the resulting antibodies recognized SRBC including the extracellular epitope in their natural conformation. In fact, the skilled in the art apparently know so well about this method, for example, in the newly submitted evidence by applicants, *Sheffer et al* immunized mice with cells positive for BCRP

mRNA expression for production of antibodies that bind BCRP protein, even though they have not found the one that recognizes the extracellular portion at the time of the publication, they indicate that they are making efforts to obtaining such antibody (last paragraph).

Third, the specification fails to teach any new method that is different from the teaching of *Ross et al*, in fact, the specification teaches that the Kohler method could be used in producing the instantly claimed antibody.

Fourth, the claims only require that the antibody recognizes an extracellular portion of a BCRP, thus, even if the antibodies taught by *Ross et al* were prepared with a purified protein that has changed its natural conformation, the antibodies would still comprise those that recognize the extracellular epitope of the BCRP. In fact, this is clearly taught in the *Niman* reference.

Niman et al teach the method of making monoclonal antibody against immunogenic polypeptides and oncoprotein ligand (abstract, claims 1-9), thus, the antibody has to recognize the extracellular portion of a protein. *Niman et al* acknowledged the art-known method of using whole cell for immunization (column 3, lines 65-67), and further teach that using a polypeptide (a partial protein), even if it is synthetic, if the amino acid sequence is correspondent to the desired epitope, the produced monoclonal antibodies would react with the intact protein under a variety of reaction conditions "BECAUSE THE RECOGNITION IS LARGELY CONFORMATIONALLY INDEPENDENT", which including the condition of recognizing a *native* protein (in its natural conformation, column 16, lines 9-33, particularly line 27).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the methods taught by *Ross et al* and *Niman et al* to make an antibody to BCRP with a reasonable expectation of success. The ordinary skilled in the art would have been motivated to do so because *Ross et al* teach the utility of the antibody in research and clinic (column 2, lines 30-34), and it is within the knowledge of the skill for various methods of antibody production and the property of antibodies produced. Thus, the claimed invention as a whole was *prima facie* obvious, and the rejection stands.

The newly submitted claims 21, 22, 25, and 26 are drawn to polyclonal or monoclonal antibodies, which have been taught by both *Ross et al* and *Niman et al* as discussed above. Therefore, the rejection applies to the new claims.

Claims 16, 17, and 21-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Ross et al* (US 6,313,277, IDS/AA) and *Niman et al* (US 5,563,247), as applied to claims 16, 17, 21, 22, 25, and 26 above and further in view of *Godfrey et al* (US 6,528,623).

Claims 23, 24, 27, and 28 are drawn to an isolated BCRP antibody that is chimeric, preferably humanized.

The combined teachings of *Ross et al* and *Niman et al* do not disclose a chimeric or humanized antibody.

Godfrey et al teach an antibody to a receptor on the surface of activated CD4+ T cells, preferably the antibody is humanized (abstract, and claim 1). *Godfrey et al* teach

the humanized antibodies are less likely to cause immunological response when used in human therapy (column 26, lines 48-58). They also teach methods of producing such chimeric, humanized antibodies (columns 19-22, § B).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Ross et al* and *Niman et al* with that of *Godfrey et al* to make an antibody to BCRP with a reasonable expectation of success. The ordinary skilled in the art would have been motivated to do so because the humanized antibodies are suitable for in vivo use in humans. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
May 15, 2003

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER